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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/927,697	08/09/2001	Yoshihide Iwaki	GY-YY-5095 / 500569.20073	6474

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EXAMINER	
GOLDBERG, JEANINE ANNE	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 03/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/927,697	IWAKI ET AL.	
	Examiner	Art Unit	
	Jeanine A Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to the papers filed August 9, 2001. Currently, claims 1-16 are pending.

Priority

2. This application claims priority to Japan 2000-241773 and Japan 2001-161199, filed 8/9/00 and 5/29/01, respectively.

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119 as follows:

It is noted, however, that applicant has not filed a certified copy of the Japan 2000-241773 and Japan 2001-161199 application as required by 35 U.S.C. 119(b).

Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d) prior to declaration of an interference, a translation of the foreign application should be submitted under 37 CFR 1.55 in reply to this action.

Sequence Rules

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

It is noted that the specification contains sequences which are not identified by SEQ ID NO:. For example, page 18 and 23, contain probe molecules which are not identified by SEQ ID NO:. Appropriate correction is required.

Claim Objections

4. Claim 16 is objected to under 37 CFR 1.75 as being a duplicate of claim 8. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim 16 and 8 are identical.

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-8, 16 are indefinite over the recitation "to produce covalent bonding" in lines 10 of Claim 1 because it is unclear whether a covalent bond if formed or whether a covalent bond may be formed. Furthermore, it is unclear between what two elements a covalent bond is formed. It is unclear whether a covalent bond is formed

between the probe and the reactive group or the probe and the solid carrier via the reactive group.

B) Claim 1-16 are indefinite because the claim fails to contain a final process step which relates back to the preamble. The preamble states that the method is for preparing a micro-array for analysis of DNA but the final process step is washing the surface of the solid carrier with an aqueous medium. Therefore the claims are unclear as to whether the method is a method of preparing a micro-array or washing the surface of a solid carrier.

C) Claims 1-16 are indefinite over the recitation "washing the surface of the solid carrier with an aqueous medium to remove the thickening agent from the surface of the solid carrier" because it is unclear whether the claim merely requires a wash step or whether the claim is directed to removing all of the thickening agent. Thus, the metes and bounds of the claimed invention are unclear.

D) Claims 7, 15 are indefinite over the recitation "each of the aqueous solutions has a viscosity essentially identical to each other" because it is unclear what is encompassed by "essentially identical." Essentially identical is a relative term which has not been defined by the instant specification. Therefore, the metes and bounds of the recitation are unclear.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1, 7-10, 12-13, 15-16 are rejected under 35 U.S.C. 102(e) as being anticipated by Blanchard (US Pat. 6,028,189, February 22, 2000; filed March 20, 1997). The claim requires that probe molecules are nucleic acid fragments. A nucleic acid fragment encompasses a single nucleotide monomer. Blanchard teaches a method of preparing micro-arrays which comprises (a) spotting onto a solid carrier an aqueous solution which contains a thickening agent and probe molecules having a reactive group to produce covalent bonding wherein the probe molecules may be a fragment of a nucleic acid, namely a single nucleotide monomer (b) spotting a second aqueous solution comprising a thickening agent and probe molecules; incubating the solid carrier having the aqueous solutions on the surface to produce the covalent bond and washing the surface of the solid carrier with an aqueous medium to remove the thickening agent from the surface of the solid carrier. Specifically, Blanchard teaches a method of assembling arrays of oligonucleotides on a solid support which couples a first nucleotide monomer to a second nucleotide monomer in a high surface tension solvent, such as propylene carbonate (col. 2, lines 48-55). The method of step-by-step synthesis of an array of different chemical compounds at microdropsized loci, where each compound is covalently attached to the surface of a substrate comprises (a) spotting at least one microdrop of a first reagent in propylene carbonate to said surface

which is chemically prepared to react with said first reagent to covalently attach said reagent to said substrate; (b) spotting onto the solid carrier in an area other than the area in which the aqueous solution was spotted, namely displacing the dispenser relative to the surface to apply a second microdrop; (c) allowing the substrate to form covalent bondings; (d) washing said carrier substrate to remove unattached reagents (col. 3, lines 25-50)(limitations of Claim 1a-d). The high surface tension solvent for the nucleotide monomers can be propylene carbonate which has a high boiling point, high viscosity, and high surface tension such that the solvent is amenable to a microfabricated ink-jet pump apparatus. Blanchard teaches that suitable solvents include propylene carbonate; acetonitrile; ethylene carbonate, HMPA and dimethyl sufoxide (col. 4, lines 65-68). Propylene carbonate has a viscosity of 2.5 centipoise (col. 4, lines 60-65)(limitations of Claim 2). It is noted that the abbreviation cP denotes a unit of viscosity equal to a centipoise, also equal to one millipascal second (mPa s). Moreover, the synthesis method exist for the covalent bond formation between the 5' positions of two nucleotide monomers, or between the 5' position of a nucleotide monomer and the 5' position of an oligonucleotide chain (col. 5, lines 35-40)(limitations of Claim 12-13). The number of cycles is indicative of the length of the oligonucleotides (col. 9, lines 12-16)(limitations of Claim 8, 16). As provided in Example II, two dimensional oligonucleotide arrays were synthesized. On a glass microscope slide, the slide was derivitized by treating with glycidoxypropyl silane and tetraethylene glycol (col. 11, lines 40-45). Using ink jets, a 0.1 molar solution of one of the four nucleotide phosphoramidites was dissolved in propylene carbonate, namely an

aqueous solution with a thickening agent (col. 11, lines 50-58). A 42pL drop was delivered to the glass slide and the reaction was allowed to proceed for 30 to 60 seconds under an inert atmosphere, namely a coupling step. The slide was rinsed with acetonitrile then dipped in iodine, pyridine and water, ie. washing the surface of the carrier to remove some thickening agent (col. 11-12).

7. Claims 1, 3, 6-9, 11, 14-16 are rejected under 35 U.S.C. 102(e) as being anticipated by Abrams et al (US Pat. 6,492,118, December 10, 2002, filed August 28, 2000).

Abrams et al. (herein referred to as Abrams) teaches a method of immobilizing ligands on solid supports which includes providing a solid support containing an immobilized latent thiol group, activating the thiol group and contacting the activated thiol group with a nucleic acid comprising an acrylamide functional group and forming a covalent bond between the two groups. Abrams teaches a method of forming an array on an acrylate slide (Example 5, col. 26, lines 65-67). Acrylamide modified oligonucleotide probes are crosslinked to polyacrylamide gel support (col. 26-27). Acrylamide modified oligonucleotide probes were spotted onto thiol containing gel-coated slides and allowed to react. The slides were washed to remove unbound probe with TE+0.2M sodium chloride and TE pH8 (col. 27, lines 10-15)(limitations of Claim 6, 14). Specifically, acrylamide is a thickening agent and a water soluble polymer (limitations of claim 3, 11). The oligonucleotides containing an acrylamide are fixed in an aqueous solution prior to attachment to the solid support. Therefore, spotting is

performed in several locations using an aqueous solution containing a thickening agent (col. 27-28)(limitations of Claim 1, 7, 17). Abrams also teaches that his invention is directed to the product formed by the method of forming a solid support (limitations of Claims 8, 16). With respect to Claim 9, oligonucleotides are electrically chargeable.

8. Claims 1, 3-5, 8-9, 11, 15-16 are rejected under 35 U.S.C. 102(e) as being anticipated by Makino et al (US Pat. 6,399,305, June 4, 2002, filed June 7, 2000).

Makino et al. (herein referred to as Makino) teaches a method of producing DNA chips. Makino teaches DNA fragments having a reactive group on one end can be fixed onto an electroconductive substrate by spotting onto the substrate an aqueous solution containing the DNA fragment (col. 6, lines 40-45). The aqueous solution may contain a viscosity increasing additive such as sucrose, poleythlene glycol or glycerol (col. 6, lines 47-50)(limitations of Claim 3). The DNA fragment is fixed onto the substrate by covalent bonding (col. 6, lines 55-56). After the incubation is complete, the free DNA fragment is washed (col. 6, lines 56-58). Inherently, the thickening agent will be also washed away to some extent. In one specific example, Example 6-1, Makino teaches preparing a PNA chip on a gold electrode surface by forming a free vinylsulfonyl group on the electrode surface; spotting aqueous solution; allowing the solution to stand; and finally removing the free PNA fragments by washing with distilled pure water (col. 19-20)(limitations of Claim 4-5).

9. Claims 1-3, 7-11, 15-16 are rejected under 35 U.S.C. 102(e) as being anticipated by Van Ness et al (US Pat. 6,248,521, June 19, 2001; filed July 21, 1998).

Van Ness et al. (herein referred to as Van Ness) teaches a method of spotting nucleic acids on a silcon wafer or glass slide. Van Ness teaches printing (delivering or applying) oligonucleotides on a solid substrate in a regular pattern and allowing the polymers to dry. Van Ness teaches that solutions with viscosity enhancing chemicals such as glycerol provide especially improved handling capabilities using hydrophilic surfaces (col. 7, lines 15-17). Van Ness teaches that the 5' amine on the oligonucleotide may be reacted with a cross-linker such that the oligonucleotide is covalently attached to the polymer coating on the solid support. A "typical procedure" uses a solution of nucleic acid uniformly mixed in 57% glycerol and printed onto the solid support (col. 7, lines 30-35). The arraying solution is made with 56% glycerol and 44% water colored with blue food color (col. 19, lines 58-60). An arraying tip is used to spot solution into many microspots on a silicon wafer (col. 19, lines 59-63). The array is then washed in water (col. 20, lines 10-20). Inherently, the thickening agent and water-soluble polymer, namely glycerol, will be also washed away to some extent. It is noted that the abbreviation cP denotes a unit of viscosity equal to a centipoise, also equal to one millipascal second (mPa s). A fluid comprising 50% water and 50% glycerol, and having a viscosity of about 5 centipoises. A fluid comprising 38% water and 62% glycerol, and having a viscosity of about 10 centipoises. Therefore, based upon the examiner's calculation a solution of 56% glycerol and 44% water falls within the scope of claim 2.

Conclusion

10. No claims allowable over the art.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

J. Goldberg

Jeanine Goldberg
March 6, 2003

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